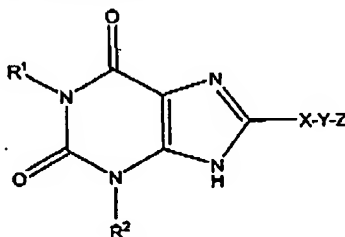


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APPENDIX A

CLEAN COPY OF CLAIMS AS AMENDED HEREIN

1. A process for the preparation of a compound of Formula I:



Formula I

wherein:

R<sup>1</sup> and R<sup>2</sup> are independently optionally substituted alkyl;

X is pyrazol-4-yl;

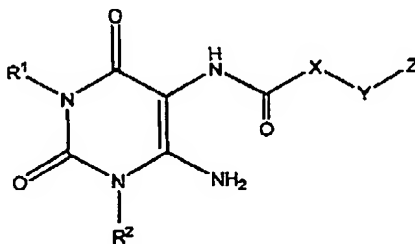
Y is a covalent bond or lower alkylene; and

Z is optionally substituted monocyclic aryl or optionally substituted monocyclic

heteroaryl;

comprising;

cyclizing a compound of the formula (3):



(3)

wherein R<sup>1</sup>, R<sup>2</sup>, X, Y, and Z are as defined above.

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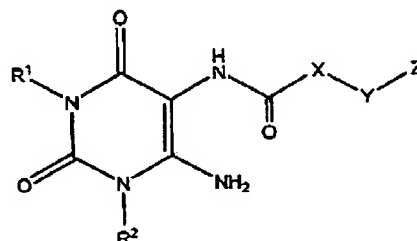
2. The process of claim 1, wherein the compound of formula (3) is cyclized in an inert solvent in the presence of a base.

3. The process of claim 2, wherein the inert solvent is methanol and the base is aqueous sodium hydroxide solution.

4. The process of claim 3, wherein  $R^1$  and  $R^2$  are independently lower alkyl, Y is methylene, and Z is optionally substituted phenyl.

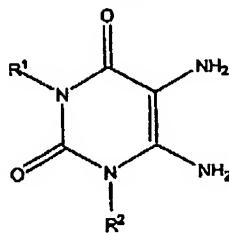
5. The process of claim 4, wherein  $R^1$  is n-propyl,  $R^2$  is ethyl, and Z is 3-trifluoromethylphenyl.

6. The process of claim 1, wherein the compound of formula (3):



(3)

is prepared by a method comprising contacting a compound of the formula (2);

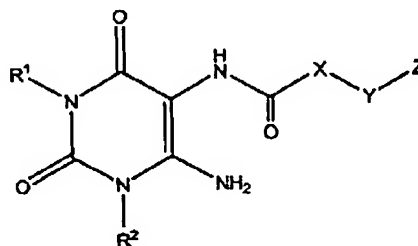


(2)

with a compound of the formula  $Z-Y-X-CO_2H$  in the presence of a carbodiimide or with a compound of the formula  $Z-Y-X-C(O)Hal$ , where Hal is chloro or bromo.

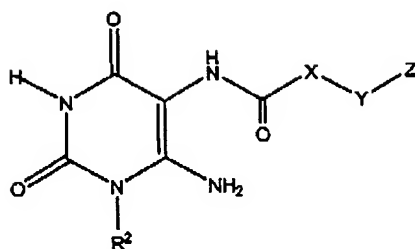
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7. The process of claim 6, wherein the compound of formula (3) is reacted with a compound of the formula  $Z-Y-X-CO_2H$  in methanol.
8. The process of claim 7, wherein the carbodiimide is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.
9. The process of claim 6, wherein the compound of formula (3) is reacted with a compound of the formula  $Z-Y-X-C(O)Cl$ .
10. The process of claim 9, wherein the reaction is carried out in an inert solvent in the presence of a tertiary base.
11. The process of claim 10, wherein the inert solvent is acetonitrile and the tertiary base is triethylamine.
12. The process of claim 6, wherein  $R^1$  and  $R^2$  are independently lower alkyl,  $X$  is pyrazol-4-yl,  $Y$  is methylene, and  $Z$  is optionally substituted phenyl.
13. The process of claim 12, wherein  $R^1$  is n-propyl,  $R^2$  is ethyl, and  $Z$  is 3-trifluoromethylphenyl, namely 3-ethyl-1-propyl-8-{1-[(3-trifluoromethylphenyl)methyl]pyrazol-4-yl}-1,3,7-trihydropurine-2,6-dione.
14. The process of claim 1, wherein the compound of the formula:



is prepared by a method comprising contacting a compound of the formula;

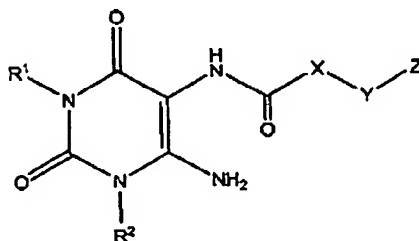
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(16)

with a compound of the formula  $R^1L$ , in which L is a leaving group.

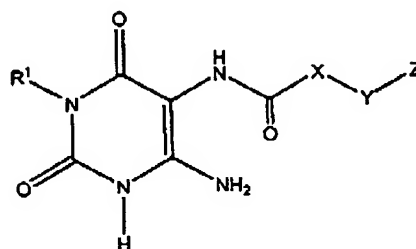
15. The process of claim 14, wherein  $R^1$  is lower alkyl optionally substituted by cycloalkyl, and L is iodo.
16. The process of claim 15, wherein the reaction is carried out in the presence of a base in an inert solvent.
17. The process of claim 16, wherein the base is potassium carbonate and the inert solvent is N,N-dimethylformamide.
18. The process of claim 17, wherein  $R^1$  and  $R^2$  are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.
19. The process of claim 18, wherein  $R^1$  is n-propyl,  $R^2$  is ethyl, and Z is 3-trifluoromethylphenyl.
20. The process of claim 1, wherein the compound of the formula:



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(3)

is prepared by a method comprising contacting a compound of the formula;



(13)

with a compound of the formula R<sup>2</sup>L, in which L is a leaving group.

21. The process of claim 20, wherein R<sup>2</sup> is lower alkyl optionally substituted by cycloalkyl, and L is iodo.

22. The process of claim 21, wherein the reaction is carried out in the presence of a base in an inert solvent.

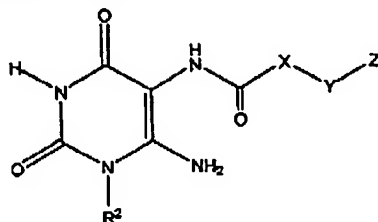
23. The process of claim 22, wherein the base is potassium carbonate and the inert solvent is N,N-dimethylformamide.

24. The process of claim 23, wherein R<sup>1</sup> and R<sup>2</sup> are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.

25. The process of claim 24, wherein R<sup>1</sup> is n-propyl, R<sup>2</sup> is ethyl, and Z is 3-trifluoromethylphenyl.

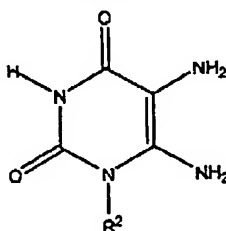
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26. The process of claim 14, wherein the compound of the formula:



(16)

is prepared by a method comprising contacting a compound of the formula:



(15)

with a compound of the formula  $Z-Y-X-CO_2H$  in the presence of a carbodiimide or with a compound of the formula  $Z-Y-X-C(O)Hal$ , where Hal is chloro or bromo.

27. The process of claim 26, wherein the compound of formula (15) is reacted with a compound of the formula  $Z-Y-X-CO_2H$  in methanol.

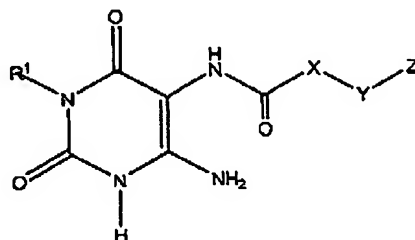
28. The process of claim 27, wherein the carbodiimide is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.

29. The process of claim 26, wherein the compound of formula (15) is reacted with a compound of the formula  $Z-Y-X-C(O)Cl$ .

30. The process of claim 29, wherein the reaction is carried out in an inert solvent in the presence of a tertiary base.

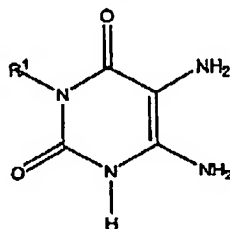
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31. The process of claim 30, wherein the inert solvent is acetonitrile and the tertiary base is triethylamine.
32. The process of claim 31, wherein  $R^1$  and  $R^2$  are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.
33. The process of claim 32, wherein  $R^1$  is n-propyl,  $R^2$  is ethyl, and Z is 3-trifluoromethylphenyl.
34. The process of claim 19, wherein the compound of the formula:



(13)

is prepared by a method comprising contacting a compound of the formula:



(12)

with a compound of the formula  $Z-Y-X-CO_2H$  in the presence of a carbodiimide or a compound of the formula  $Z-Y-X-C(O)Hal$ , where Hal is chloro or bromo.

35. The process of claim 34, wherein the compound of formula (12) is reacted with a compound of the formula  $Z-Y-X-CO_2H$  in methanol.

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36. The process of claim 35, wherein the carbodiimide is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.

37. The process of claim 34, wherein the compound of formula (12) is reacted with a compound of the formula Z-Y-X-C(O)Cl.

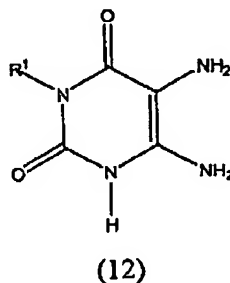
38. The process of claim 37, wherein the reaction is carried out in an inert solvent in the presence of a tertiary base.

39. The process of claim 38, wherein the inert solvent is acetonitrile and the tertiary base is triethylamine.

40. The process of claim 39, wherein R<sup>1</sup> and R<sup>2</sup> are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.

41. The process of claim 40, wherein R<sup>1</sup> is n-propyl, R<sup>2</sup> is ethyl, and Z is 3-trifluoromethylphenyl.

42. The process of claim 34, wherein the compound of the formula:



is prepared by a method comprising the steps of:

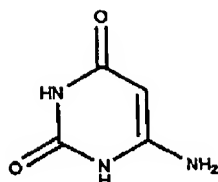
- a) contacting a compound of the formula:



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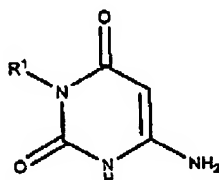
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with hexamethyldisilazane in the presence of an acid catalyst;

b) contacting the product thus formed with  $R^1L$ , where L is a leaving group, followed by;

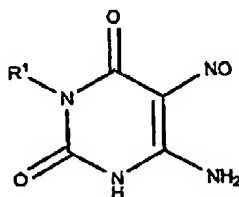
c) contacting the product thus formed:



(10)

with a mixture of sodium nitrite in acetic acid/water, and

d) contacting the product thus formed:



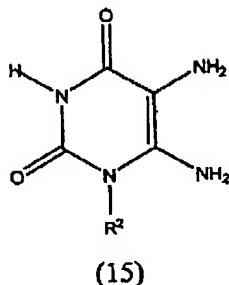
(11)

with a mixture of aqueous ammonia and sodium dithionite.

43. The process of claim 42, wherein in step a)  $R^1$  is lower alkyl, L is iodo, and the acid catalyst is ammonium sulfate.

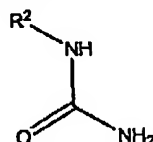
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44. The process of claim 26, wherein the compound of the formula:



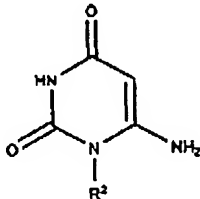
is prepared by a method comprising the steps of:

- a) contacting a compound of the formula:



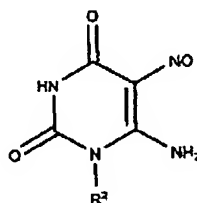
with ethyl cyanoacetate in the presence of a base in a protic solvent;

- b) contacting the product thus formed:



with a mixture of sodium nitrite in acetic acid/water; and

- c) contacting the product thus formed:

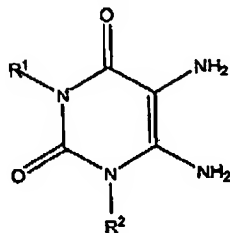


with a mixture of aqueous ammonia and sodium dithionite.

45. The process of claim 44, wherein the base is sodium ethoxide and the protic solvent is ethanol.

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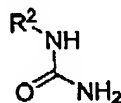
46. The process of claim 6, wherein the compound of formula:



(2)

is prepared by a method comprising the steps of:

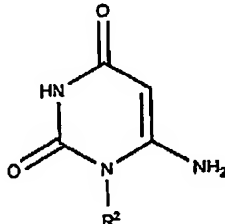
- a) contacting a compound of the formula:



(4)

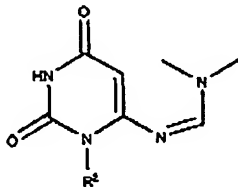
with ethyl cyanoacetate in the presence of a base in a protic solvent;

- b) contacting the product thus formed:



with the dimethylacetal of N,N-dimethylformamide;

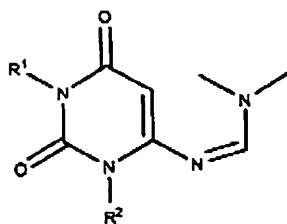
- c) contacting the product thus formed:



with a compound of formula R<sup>1</sup>L, in which L is a leaving group;

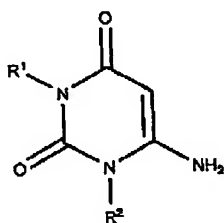
- d) contacting the product thus formed:

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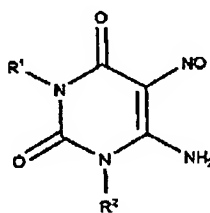
with aqueous ammonia;

- e) contacting the product thus formed:



with a mixture of sodium nitrite in acetic acid/water; and

- f) contacting the product thus formed:



with a mixture of aqueous ammonia and sodium dithionite.

47. The process of claim 46, wherein the base is sodium ethoxide and the protic solvent is ethanol.

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